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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,646	08/16/2006	Jilly Evans	21238YP	1012

210 7590 11/16/2007

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EXAMINER
BETTON, TIMOTHY E

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
11/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,646	EVANS ET AL.	
	Examiner	Art Unit	
	Timothy E. Betton	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3 sheets, 16 August 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejection(s) – 35 USC§ 112, 1ST paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

As stated in MPEP 2164.01(a), " There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue."

In re Wands, set forth the following eight factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, 1ST paragraph:

1. The nature of the invention;
2. The state of the prior art;
3. The predictability or lack thereof in the art;
4. The amount of direction or guidance present;
5. The presence or absence of working examples;
6. The breadth of the claims;
7. The quantity of experimentation needed; and
8. The level of the skill in the art.

The factors as stated above are addressed below on the basis of comparison of the disclosure and the scope of the claims directed to a use in view of the instant specification.

The current invention is directed to a method of treating atherosclerosis, comprising administering a therapeutically effective amount of a cysteinyl leukotriene 2 receptor antagonist to a patient in need of such treatment. Particular disease states, which are indicated for treatment with the instant cysteinyl leukotriene 2 receptor antagonist are atherosclerosis, atherosclerotic plaque, aortic aneurysm, pulmonary fibrosis, and cerebral edema.

However, it would not be so apparent to the skilled artisan that due experimentation was possible (notwithstanding undue experimentation) because the skilled artisan would not be so inclined as to accept on its face that the claimed cysteinyl leukotriene 2 receptor antagonist could, in fact, treat and/or palliate the disease states indicated above.

The objective of claimed invention is not elucidated with the adequate direction and guidance necessary for one of ordinary skill to determine enabling in view of the scope of use of the claimed invention. Additionally, the instant specification is underdeveloped in regard to a proper disclosure of specifically how a cysteinyl leukotriene 2 receptor antagonist would be used in a target population having disease states as cited above. The instant specification, instead, is drawn to extrapolations of hypothetical explanations of use in a patient with cerebral edema, pulmonary fibrosis, aortic aneurysm, etc. To the skilled artisan, empirical assessments of activity of a complex compound such as cysteinyl leukotriene 2 receptor antagonist drawn to the treatment of those in need of such treatment would essentially require predictable outcomes in order to sufficiently determine enabling. However, the instant specification is absent of such disclosure.

More specifically, in instant claim 5, the disclosure is drawn to a method of preventing the risk of atherosclerotic plaque. In the instant specification it cites: Thus, activation of the

CysLT1 and CysLT2 receptors on coronary smooth muscle cells may activate contraction and plaque rupture. Autocrine activation of the CysLT1 and CysLT2 receptors on the foam macrophage or interstitial mast cells may result in further release of damaging inflammatory and immune molecules. As a result, a CysLT2 antagonist, including both a CysLT2 receptor selective antagonist or dual CysLT1/CysLT2 receptor antagonist *could prevent* the endothelial cell, smooth muscle cell and inflammatory cell activation, thereby *preventing* plaque rupture (page 2, 4th full paragraph).

However, there is nothing present in the instant specification, which supports or suggests prevention of atherosclerotic plaque rupture.

Accordingly, the skilled artisan would be inclined to associate prevention of any disease with evidence of a significant reduction and/or resolve in a particular disease state in a particular target population determined to be in need of such administration. However, in order to prevent a disease, four general factors (of which three will be addressed due to direct relevance) have been determined to be of importance (The Language of Prevention, National Public Health Partnership (2006). The Language of Prevention, printed pages 1-9, especially pages 5 and 9).

(i) Through due experimentation, evidence of significant reduction in the average risk of the particular disease must be properly assessed and quantified to further determine a level of predictability. (ii) Also, the instant specification and claim disclose a complex disease state. However, the instant specification fails to provide guidance and direction in terms of how prevention would occur against the actual progression of atherosclerotic plaques. The variable susceptibilities of atherosclerotic plaques have not been elucidated in such a way that the skilled artisan would be inclined to derive prevention from the claimed subject matter. (iii) Accordingly,

a plainly identified target population is tantamount in the way of determining the predictability of any level of prevention via treatment. The instant invention is of such a nature that a plainly identified target population for any of the disease states as enumerated would sufficiently provide evidence of a measure, order, and/ or degree of prevention (quantification). However, the instant specification and claims are absent of any disclosure or embodiments directed specifically to atherosclerotic plaque.

It is in this regard that Applicant is directed to the MPEP at §2164.08. All questions of enablement are evaluated against the claimed subject matter. Concerning the breadth of a claim relevant to enablement, the only relevant concern is whether the enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims. The determination of the propriety of a rejection based upon the scope of a claim relative to enablement involves the determination of how broad the claim is with respect to the disclosure and the determination of whether one skilled in the art is enabled to use the entire scope of the claimed invention without undue experimentation.

Applicant fails to provide a sufficiently suitable example of the claimed compound in treating the disease states as enumerated above. While a lack of a working embodiment cannot be the sole factor in determining enablement, the absence of substantial evidence commensurate in scope with the presently claimed subject matter, in light of the unpredictable nature of the art and the direction that Applicant has presented, provides additional weight to the present conclusion of insufficient enablement in consideration of the Wands factors as a whole. The instant specification lacks disclosure or teaching of manner and process of using the presently claimed compounds for achieving the objective of a method of treating. Nowhere does the

specification disclose the manner or procedure of using the presently claimed compound for preventing the onset of the same such that the skilled artisan would have been invested with at least a. reasonable expectation of success in actually achieving such an objective without the burden of an undue level of experimentation.

The basis for the present rejection is not simply that experimentation would be required, since it is clear from the state of the pharmaceutical and chemical arts that experimentation in this particular art is not at all uncommon, but that the level of experimentation required in order to practice this aspect of the invention in the absence of any enabling direction by Applicant would be undue.

In view of the discussion of each of the preceding factors, the level of skill in the art is high and is at least that of physician with several years of experience in the specialized art.

As the cited art and discussion of the above factors establish, practicing the claimed method in the manner disclosed by Applicant would not invest the skilled artisan with a reasonable expectation that the objective of treating (and preventing atherosclerotic plaque) could be achieved. In order to actually achieve such results, it is clear from the discussion above that the skilled artisan could not rely upon Applicant's disclosure as required by 35 U.S.C. 112, first paragraph, and would have no alternative recourse but the impermissible burden of undue experimentation in order to practice the full scope of the presently claimed invention.

Claim Rejection(s) – 35 USC§ 112, 1ST paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 6,7,9-11, 13-15, and 17-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Instant claims 1-3, 6,7,9-11, 13-15, and 17-19 cite an organic chemical administered but is disclosed as claimed solely via function. This is not a sufficient description and/or explanation of the instant subject matter in view of the scope of claimed invention. The cited antagonists of the claims *supra* are not described by way of any written description except for the instant claims (which are not listed in this rejection), which do adequately elucidate a particular chemical moiety classified as an antagonist. The limitations of 1-3, 6,7,9-11, 13-15, and 17-19 would instantly be apparent to one of ordinary skill as failing to adequately and specifically, (i.e., actual chemical name and/or other representative explanations of moieties) describe the cysteinyl leukotriene 2 receptor antagonist.

Accordingly, the written basis is absent in regard to instant claims 1-3, 6,7,9-11, 13-15, and 17-19. The current invention is drawn to methods of treating, preventing, and reducing certain disease states as disclosed. However, it would not be clear, concise, and/or exact to the

skilled artisan as to which particular antagonist is being disclosed in the instant claims *supra.* Additionally, with the limitations as disclosed in instant claim 2, it is unclear whether the antagonists are directed to the same moiety or two different moieties of antagonists. The instant claims such as claims 4, 8, 12, etc. cite one consistent moiety of a cysteinyl leukotriene 2 receptor antagonist. However, it is not so apparent that this moiety as disclosed is indicated for instant claims 1-3, 6,7,9-11, 13-15, and 17-19.

Conclusion

Claims 1-20 stand rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy E. Betton whose telephone number is (571) 272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a
USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TEB

A. H. Marschel 1/13/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER